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PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:

Paul C. Anderson *et al.*

Serial No.: 09/732,439

Filed: December 7, 2000

For: TRANSGENIC MAIZE WITH
INCREASED PROLINE CONTENT (AS
AMENDED)

Group Art Unit: 1638

Examiner: Cynthia E. Collins

Atty. Dkt. No.: DEKM:184USD1

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37 C.F.R. §1.8

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May 31, 2005
Date

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Robert E. Hanson

REPLY BRIEF

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Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

Sir:

Appellants hereby submit an original and two copies of this Reply Brief in response to the Examiner's Answer, dated March 28, 2005. It is believed that no fees are due in connection with this paper; however, should any fees be due the Commissioner is authorized to withdraw the appropriate fees from Fulbright & Jaworski Deposit Account No. 50-1212/ DEKM:184USD1.

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I. REAL PARTY IN INTEREST

The real party in interest is Monsanto Company, the parent company of assignee DeKalb Genetics Corp.

II. RELATED APPEALS AND INTERFERENCES

There are no interferences or appeals for related cases.

III. STATUS OF THE CLAIMS

Claims 1-58 were originally filed. Claims 59-96 were added and claims 1-58 were cancelled in the Preliminary Amendment mailed on December 7, 2000. In response to a Restriction Requirement, Appellants elected Group I, comprising claims 59-63 and 72-73. Claims 64-71 and 74-96 were subsequently withdrawn from consideration by the Examiner as drawn to non-elected subject matter.

An Amendment Under 37 C.F.R. §1.116 was filed with the first Appeal Brief on March 12, 2004 amending claim 73. A second Amendment Under 37 C.F.R. §1.116 was filed on November 23, 2004 amending claim 63.

Claims 59-63 and 72-73 are currently pending. A copy of the pending claims as they stand on appeal is attached as Appendix 1.

IV. STATUS OF AMENDMENTS

Amendments Under 37 C.F.R. §1.116 were filed on March 12, 2004 and November 23, 2004 and have been entered by the Examiner. No other claim amendments have been made.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The invention relates to methods for the creation of transgenic monocot plants and seeds that display increased water stress resistance or tolerance. Specification at page 3, lines 20-24. More particularly, it concerns expression in monocots of an enzyme that catalyzes the synthesis of the osmoprotectant proline. Specification at page 3, lines 26-29, and page 4, line 8.

VI. GROUND OF REJECTION TO BE REVIEWED ON APPEAL

(A) Are claims 59-63 and 72-73 properly rejected under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description in the specification?

(B) Are claims 59-63 and 72-73 properly rejected under 35 U.S.C. § 112, first paragraph, as lacking enablement in the specification?

(C) Are claims 61-63 properly rejected under 35 U.S.C. § 112, second paragraph, as being indefinite?

(D) Are claims 59-61, 63, 72 and 73 properly rejected under 35 U.S.C. § 102(e) as being anticipated by Verma *et al.* (U.S. Patent 5,639,950)?

(E) Are claims 59-63 and 72-73 properly rejected under 35 U.S.C. § 103(a), as being obvious over Verma *et al.* (U.S. Patent 5,639,950) in view of Rayapati *et al.* (*Plant Physiology*, 1989, vol. 91, pages 581-586) and Appellants allegedly admitted prior art?

VII. REPLY

A. The Claims Do Not Lack Written Description

The Answer asserts in response to Appellants Brief that written description is lacking because the claims allegedly are not limited to a specific nucleic acid sequence encoding an enzyme that catalyzes biosynthesis of proline, because “disclosure of four sequences encoding

two type [sic] of enzymes involving proline biosynthesis is not representative of the genus of sequences used to make the claimed transgenic plant,” and because two of the references showing proline biosynthesis genes were either published after the filing date or were not made of record in earlier responses.

Regarding whether the claims require a specific proline biosynthesis gene, it is noted that the claims require no more than what was already in the prior art in terms of proline biosynthesis genes. All that is required by the claims is that proline be biosynthesized and such genes serving this function were known in the art. The Examiner has provided no basis to conclude that the known genes are not representative of the sequences used in the claims. Among such known genes, for example, are the mothbean cDNA clone encoding a bifunctional enzyme delta1-pyrroline-5-carboxylate synthetase described by Verma *et al.* (**Exhibit A**) and the soybean homologue of delta1-pyrroline-5-carboxylate synthetase described by Hu *et al.* (**Exhibit B**). The prior art rejection acknowledges that such delta1-pyrroline-5-carboxylate synthetase enzymes *inherently yield drought tolerant plants*. See Answer at p. 24, 30. Thus, based on this admission alone, these two sequences represent examples acknowledged to function to produce a drought tolerant plant according to the invention. Despite unsupported statements to the contrary, no basis has been provided to show why these examples alone are not representative of the sequences recited by the claims.

Still other genes encoding enzymes biosynthesizing proline were known and the Examiner has failed to show why these do not describe the claims as well. For example, pyrroline-5-carboxylate reductases from humans (**Exhibit L**) and yeast (**Exhibit M**) were known. Additional examples of pyrroline-5-carboxylate reductase from *Arabidopsis* (**Exhibit K**) and pea (**Exhibit N**) were also known but disregarded in the Answer because the former

reference was published a few months after the current filing date and the latter reference was not earlier entered by the Examiner in the record. However, both references demonstrate the contemporaneous knowledge of those of skill in the art. The first reference by Verbruggen *et al.*, for example, was submitted for publication on January 21, 1993, well before the filing date. **Exhibit L**, p. 779. The second reference by Williamson and Slocum, while not entered on the record, was published prior to filing and is evidence of the knowledge of the skill in the art. In considering written description it is specifically the burden of the Examiner to take into account the knowledge of those of skill in the art. See *Wang Labs., Inc. v. Toshiba Corp.*, 993 F.2d 858, 863 (Fed. Cir. 1993) (holding that written description is reviewed from the perspective of one of skill in the art at the time the application is filed). It is thus submitted that this evidence may not be properly disregarded.

B. The Claims Are Enabled

The Answer asserts that enablement is lacking because the claims do not merely require transgenic monocots expressing enzymes synthesizing proline, but rather require drought tolerant plants. Answer at p.18. However, on pages 22-23 of the Answer the Examiner specifically acknowledges that Appellants are enabled for monocot transformation and heterologous gene expression and that expression of a delta1-pyrroline-5-carboxylate synthetase in monocots inherently results in a water stress tolerant plant. The Answer therefore acknowledges enablement of at least two embodiments based on the delta1-pyrroline-5-carboxylate synthetases of Verma *et al.* (**Exhibit A**) and Hu *et al.* (**Exhibit B**). These examples alone establish enablement of the claims and no basis has been provided to conclude otherwise.

Still further, statements to the contrary in the Answer notwithstanding, the success of Appellants in expressing other compatible osmoprotectants in monocots to achieve resistance to

a reduction in water availability is evidence demonstrating enablement. The two issued patents showing transgenic plants expressing the osmoprotectants mannitol (see US Patent 5,780,709, **Exhibit D**) and glycine betaine (see U.S. Patent 6,281,411, **Exhibit C**), for example, claim priority to the same parent application as the current case and the latter patent is the parent application of this case. Proline, like mannitol and glycine betaine, is a known endogenous osmoprotectant that has long been identified as playing a role in plants under water deficit. The prior studies demonstrate that accumulation of such osmoprotectants yields resistance to osmotic stress. Combined with studies showing that significant increases in proline are observed under water deficit (**Exhibit E**) and salt stress (**Exhibit F**), that proline serves as an osmoprotectant in diverse organisms (**Exhibit G**), and that increased proline accumulation is observed in drought-resistant tobacco cultivars compared to the drought-sensitive cultivars (**Exhibit H**), as well as the acknowledgement of enablement for increased drought tolerance by expression of delta-pyrroline-5-carboxylate synthetase, satisfaction of enablement has more than been demonstrated pursuant to §112, first paragraph.

C. The Claims Are Not Indefinite

The Answer maintains the indefiniteness rejection of claim 61 and claims dependent thereon for the use of the term “increased.” Specifically, it is stated that, although a plain reading of the claim is not unclear, when read with the specification, alternate meanings could be envisioned. Answer at p. 24. For example, it is asserted that “increased” could be viewed relative to the level of endogenous enzyme in a transgenic maize plant or relative to the enzyme produced by a plant under non-stress conditions. Appellants respectfully submit that such a strained interpretation is contrary to the standard under §112, second paragraph. Claims must be

given their reasonable meaning as one of skill in the art would understand them. Here, claim 61 reads as follows:

61. A fertile transgenic *Zea mays* plant comprising a recombinant DNA segment comprising a promoter operably linked to a first DNA segment encoding an enzyme which catalyzes the synthesis of the osmoprotectant proline, wherein the first DNA segment *is expressed so that* the level of the enzyme is *increased* in the transgenic *Zea mays* plant, and wherein the recombinant DNA segment is heritable.

(emphasis added)

As can be seen from the text of the claim, the only reasonable meaning of “increased” is that the enzyme is increased relative to a *Zea mays* plant not expressing the DNA segment encoding an enzyme synthesizing proline. The frame of reference is thus the underlying plant that does not express the DNA segment. How much endogenous enzyme is being expressed and whether the plant is stressed is irrelevant, because enzyme will be increased by expression over whatever the pre-existing level was, regardless of the amount. It is therefore respectfully submitted that the indefiniteness rejection is completely unfounded.

D. The Claims Were Not Properly Rejected Under 35 U.S.C. §102(e)

The Answer acknowledges that Verma I does not include the terms “maize,” *Zea mays*,” “corn” or “monocot,” yet somehow concludes that transgenic monocot plants are anticipated because the Verma II reference supplements these shortcomings. Answer at p. 26. It is respectfully submitted that this analysis is legally flawed. The Answer attempts to support the effectiveness of the filing date of Verma I based on elements only found in the Verma II reference, which is *not prior art* as of its filing date. The relevant issue is the sufficiency of Verma I. This reference does *not disclose monocots*. Thus, regardless of what Verma II discloses, Verma I does not disclose all elements of the claims and does not anticipate the claims.

It is well settled that a genus does not anticipate a species yet that is precisely what the Answer would hold. The Answer alleges that because Verma I refers to plants generally, monocot plants must also be disclosed when combined with the new matter of Verma II. Under any view, the approach taken does not set forth a proper anticipation rejection.

E. The Claims Are Not Obvious

The Answer maintains the obviousness rejection largely on the reasoning used in the anticipation rejection. Specifically, the new matter in Verma II regarding monocot plants is used to supplement Verma I and somehow render it effective as prior art. Again, however, *Verma II* is not prior art as of its actual filing date. Verma I does not disclose monocot plants, as acknowledged by the Examiner. The fact that an application was filed after Appellants' priority date adding this element does not retroactively render it sufficient for this subject matter. The motivation to combine and all elements of the claims must be found in the *prior* art. Conclusory statements about Verma II being effective as of the filing date of Verma I cannot satisfy this requirement because Verma I does not disclose all elements of the claims as of the filing date.

It is further noted that even Verma II does not disclose an actual transgenic monocot plant. The defects of Rayapati *et al.* are not cured based on this reference. The combined references do not teach fertile, transformed corn. The references have further not been shown to provide a motivation to arrive at the claimed invention, let alone a reasonable expectation of success in doing so. The rejection is therefore completely without support.

VIII. CONCLUSION

It is respectfully submitted, in light of the above, that none of the claims are properly rejected. Therefore, Appellants request that the Board reverse the pending grounds for rejection.

Respectfully submitted,



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Date: May 31, 2005

APPENDIX 1

59. A transformed monocot plant, which plant is substantially tolerant or resistant to a reduction in water availability, the cells of which comprise a recombinant DNA segment comprising a preselected DNA segment encoding an enzyme which catalyzes the synthesis of the osmoprotectant proline, wherein the enzyme is expressed in an amount effective to confer tolerance or resistance to the transformed plant to a reduction in water availability.

60. The transformed plant of claim 59 wherein the transformed plant has an improved osmotic potential when the total water potential of the transformed plant approaches zero.

61. A fertile transgenic *Zea mays* plant comprising a recombinant DNA segment comprising a promoter operably linked to a first DNA segment encoding an enzyme which catalyzes the synthesis of the osmoprotectant proline, wherein the first DNA segment is expressed so that the level of the enzyme is increased in the transgenic *Zea mays* plant, and wherein the recombinant DNA segment is heritable.

62. The fertile transgenic *Zea mays* plant of claim 61, wherein the recombinant DNA segment further comprises a second DNA segment encoding an amino terminal chloroplast transit peptide operably linked to the first DNA segment.

63. A seed produced by the transgenic plant of claim 61 comprising said recombinant DNA segment.

72. A transformed monocot plant regenerated from the transformed plant cells obtained by the method of claim 64.

73. A transgenic seed of the transformed plant of claim 72 which comprises the expression cassette.



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May 31, 2005 Date	 Robert E. Hanson

RE: *SN 09/732,439 entitled "TRANSGENIC MAIZE WITH INCREASED PROLINE CONTENT (AS AMENDED)" – Paul C. Anderson et al.*
Our Ref. DEKM:184USD1; Client Ref. 51207 US 12

Commissioner:

Enclosed for filing in the above-referenced patent application are:

1. A Reply Brief (original and 2 copies);
2. A return postcard to acknowledge receipt of these materials. Please date stamp and mail this postcard.

If the check is inadvertently omitted, or should any additional fees be required under 37 C.F.R. §§ 1.16 to 1.21 for any reason relating to the enclosed materials, the Commissioner is authorized to deduct said fees from Fulbright & Jaworski Deposit Account No. 50-1212/DEKM:184USD1.

Respectfully submitted,

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REH/ddr
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